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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/718,355	ROULEAU ET AL.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *20 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *7,8,10 and 14-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,8,10 and 14-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *IDS: 6/2001*.

DETAILED ACTION

Election/Restrictions

1. Claims 7, 8, 10, and 14-30 are pending in the instant application. Applicant's election without traverse in the paper dated 9/22/2003 is acknowledged. An action on the merits follows.

Specification

2. The sequence listings filed December 9, 2002 and September 22, 2003 are objected to under 35 U.S.C. 132 because they introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: For example, SEQ ID NO: 23 contains N's at certain positions (directed to any of the four nucleotide bases A, T, G, or C) whereas the originally filed SEQ ID NO: 23 contained a specific nucleotide base at the position. This effectively broadens the disclosure of SEQ ID NO: 23, however no explanation has been given as to why this amendment to the sequence listing was made. If this was a mistake in the filing of the original sequence listing that applicant's intended to rectify in the filing of the substitute sequence listing, there must be an indication in the originally filed disclosure that one of skill in the art, reading the originally filed disclosure, would be able to surmise the correct sequence of SEQ ID NO: 23 (see for example: MPEP 2163 [R-1], section B: 'New or Amended claims': which states:

> An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction. In re Oda, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971). With respect to the correction of sequencing errors in applications disclosing nucleic acid and/or amino acid sequences, it is well known that sequencing errors are a common problem in molecular biology. See, e.g., Peter Richterich, Estimation of Errors in Raw' DNA Sequences: A Validation Study, 8 Genome Research 251-59 (1998). If an application as filed includes sequence information and references a deposit of the sequenced material made in accordance

with the requirements of 37 CFR 1.801 et seq., amendment may be permissible. Deposits made after the application filing date cannot be relied upon to support additions to or correction of information in the application as filed. Corrections of minor errors in the sequence may be possible based on the argument that one of skill in the art would have resequenced the deposited material and would have immediately recognized the minor error. Deposits made after the filing date can only be relied upon to provide support for the correction of sequence information if applicant submits a statement in compliance with 37 CFR 1.804 stating that the biological material which is deposited is a biological material specifically defined in the application as filed.

It is noted that the examiner requested an explanation (in the paper filed 3/25/2003) of each sequence change in the substitute sequence listing to be able to assess which/if any sequences, added new matter to the disclosure. As applicant's have not yet provided such explanation, and in order to expedite prosecution of the instant application, the objection is made with respect to every sequence submitted in the substitute sequence listing as it is extremely burdensome for the examiner to determine, by site alone, which sequences in the 157 page and 200 page, respectively, substitute sequences listings contain changes and which do not. Applicant is requested to provide an explanation as to which sequences were changed, and why, as well as an explanation as to which sequences were added and where such newly added sequences find support in the specification as originally filed.

Applicant is required to cancel the new matter in the reply to this Office Action.

3. The specification is also objected to as it contains sequences not followed by an appropriate sequence identifier. For example, see page 54. An appropriate sequence identifier as set forth in MPEP, chapter 2400, must follow each and every disclosure of a sequence. Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 7, 8, 10, and 14-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 8 are indefinite as it is unclear if the compound in line 2 and test agent, in line 9 is the same or different compound. This is an important distinction as it is unclear how many different compounds are being added in the assay and thus the metes and bounds of the claim are unclear. Accordingly, the recitation of 'test agent' in claims 7 and 8 lack sufficient antecedent basis, as it is unclear if such refers to the compound in the preamble in the claim or to an additional reagent in the assay.

Claim 10 is indefinite in the recitation of "providing a screening assay which comprises a measurable SCN1A biological activity" as it is unclear how a screening assay can comprise an activity. A compound such as a protein would be expected to posses a "biological activity" however it is unclear how an assay possesses such. Accordingly, the metes and bounds of the claim are unclear.

Claims 14, 17, 19-21, and 23 are indefinite, as these claims appear to further define products and not methods, however they are dependent on method claims and assays within method claims.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 20, 21, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER Rejection.

8. The claims recite SEQ ID NOS which have been changed in the substitute sequence listing. SEQ IDNO: 23, was changed from the originally filed sequence listing. SEQ ID NO: 23 contains N's at certain positions (directed to any of the four nucleotide bases A, T, G, or C) whereas the originally filed SEQ ID NO: 23 contained a specific nucleotide base at the position. This effectively broadens the disclosure of SEQ ID NO: 23, however no explanation has been given as to why this amendment to the sequence listing was made. If this was a mistake in the filing of the original sequence listing that applicant's intended to rectify in the filing of the substitute sequence listing, there must be an indication in the originally filed disclosure that one of skill in the art, reading the originally filed disclosure, would be able to surmise the correct sequence of SEQ ID NO: 23 (see for example: MPEP 2163 [R-1], section B: 'New or Amended claims': which states:

An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of the error in the specification, but also recognize the appropriate correction. In re Oda, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971). With respect to the correction of sequencing errors in applications disclosing nucleic acid and/or amino acid sequences, it is well known that sequencing errors are a common problem in molecular biology. See, e.g., Peter Richterich, Estimation of Errors in Raw' DNA Sequences: A Validation Study, 8 Genome Research 251-59 (1998). If an application as filed includes sequence information and references a deposit of the sequenced material made in accordance with the requirements of 37 CFR 1.801 et seq., amendment may be permissible. Deposits made after the application filing date cannot be relied upon to support additions to or correction of information in the application as filed. Corrections of minor errors in the sequence may be possible based on the argument that one of skill in the art would have resequenced the deposited

material and would have immediately recognized the minor error. Deposits made after the filing date can only be relied upon to provide support for the correction of sequence information if applicant submits a statement in compliance with 37 CFR 1.804 stating that the biological material which is deposited is a biological material specifically defined in the application as filed.

It is noted that the examiner requested an explanation (in the paper filed 3/25/2003) of each sequence change in the substitute sequence listing to be able to assess which/if any sequences, added new matter to the disclosure. As applicant's have not yet provided such explanation, and in order to expedite prosecution of the instant application, the rejection is made with respect to every sequence submitted in the substitute sequence listing as it is extremely burdensome for the examiner to determine, by site alone, which sequences in the 157 page and 200 page, respectively, substitute sequences listings contain changes and which do not. Applicant is requested to provide an explanation as to which sequences were changed, and why, in reply to this office action.

9. Claims 7, 8, 10, and 14-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue (See *In re Wands,* 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). These factors include, but are not limited to:

Quantity of Experimentation Necessary
Amount of Direction and Guidance
Presence and Absence of Working Examples

Nature of the Invention
Level of predictability and unpredictability in the art

The claims are broadly drawn to assays for selecting a compound useful for treating any type of epilepsy or neurological disorder which modulates inactivation of a sodium channel or any activity of a sodium channel or any biological SCN1A biological activity, by detecting a compound that modulates inactivation of a sodium channel or any activity of a sodium channel. The claims are also broadly drawn to identifying a compound from a library of compounds, that has a therapeutic effect on any type of epilepsy or any neurological disorder by detecting a compound that modulates any SCN1A biological activity. The screening methods in the above claims are broadly drawn to administering a compound to an SCN1A sodium channel from any source, or any mammalian source, or any functional fragment thereof, including allelic variants and genomic sequences.

The specification has established an association between certain mutations in human SCN1A sodium channel and idiopathic generalized epilepsy (see pages 54-56). For example, the specification teaches that the D188V mutant shifts the state inactivation of membrane potentials to those that are slightly more positive than observed in wildtype channels. The claims, however, are drawn to compounds that modulate any SCN1A biological activity or compounds that "modulate" inactivation of or activity of a sodium channel. The recitation of "biological activity of SCN1A" broadly encompasses any activity, from generally the translation of mRNA to protein, or to binding of the polypeptide to an antibody, as well as more specific activities such as 1) the voltage dependence of activation, a measure of the strength of membrane depolarization necessary to open channels, 2) the voltage dependence of steady state inactivation, a measure of the fraction of channels available to open at the resting membrane

potential, or 3) the time course of inactivation. Furthermore, for example with respect to the recitation of claim 7, the "modulation" encompassed by the compound could be further inactivation, or a correction of inactivation ie: activation, of the sodium channel, for which the specification does not teach amino acid residues or specific nucleic acid sequences that are critical for such broadly encompassed "activities".

The specification provides no working examples of any compounds that were screened for SCN1A, nor any actual screening methods undertaken for selecting any compounds that have any effect on any "SCN1 biological activity" or any "modulation" of inactivation of sodium channel or any "modulation of sodium channel activity". The specification provides no guidance as to the critical residues that are "functional fragments" of an SCN1A sodium channel. As the term "biological activity" is so broadly defined by the specification (see pages 19-20), the germ "functional fragments" also broadly encompasses specific nucleic acid or amino acid "fragments" with a particular activity. The specification, however, has not provided any guidance as to what constitutes a "functional fragment" of an SCN1A nucleic acid sequence that would be required for expression or transcription or translation to protein. The specification has provided no guidance as to critical amino acid residues required for the SCN1A channel activity. The specification has not provided any guidance as to what constitutes a "functional fragment" of an SCN1A protein required for binding to a specific antibody. Any number and sequence of amino acids could determine specificity of binding to antibodies such that the claim encompass screening for any compound that could effect such a broad scope of activities. With respect to claims 7, 8, and 10, neither the claims nor the specification provide any guidance as to whether the compound further inactivates the sodium channel or reverses inactivation of the sodium

channel. Accordingly, the claims are broadly drawn to a screening for any compound that would have any effect whatsoever on SCN1A nucleic acids or proteins. Such nucleic acid or amino acid sequences would not necessarily have any therapeutic effect in treating any type of epilepsy or *any* "other neurological disorder". The specification teaches that symptomatic epilepsies have multiple and heterogeneous causes including brain injury, CNS infection, migrational and metabolic disorders. There is no teaching in the specification, however, that a predictable correlation can be made that modulation of SCN1A would be therapeutic in different types of epilepsies with such different causes. Further, the specification provides no predictable correlation that modulation of SCN1A or any "functional fragment" or any allelic variant or even any sodium channel would be therapeutic for the broad scope of neurological disorders encompassed by the claims, such as Alzheimer's disease, Parkinson's disease, schizophrenia, depression, bipolar disorder, etc. Additionally, with regard to "allelic variants" the claims encompass compounds which modulate a large number of sequences that have not been taught or described, as well as unknown nucleic acids and proteins.

With regard to compounds and the broad recitation of 'therapeutic" or useful for "treating", the art teaches that such compounds do not necessarily have any structure-function correlation such that a predictable association can be made with a particular class of compounds and therapy or therapeutic effect. For example, Clare (Clare et al; DDT vol. 5, 2000; pages 506-518), teaches that with regard to voltage gated sodium channels as therapeutic targets, drugs differ widely in their therapeutic effect and structure, even those have common binding determinants (see page 509, col. 1). Taylor (Taylor et al, Adv. Pharmacol. Vol. 39, pp 47-98; 1997) teaches that phenytoin, a sodium channel blocker, like anticonvulsants prevent tonic

extensor seizures in rodents from maximal electroshock and reduce the severity of seizures, but generally lack activity against clonic seizures and have little or no activity against spontaneous absence seizures in rats (see para bridging pages 74-75). Taylor also teaches, however, that some sodium channel blockers cause seizures (see page 74, para 2).

Therefore, given the lack of guidance from the specification and the unpredictability taught in the art with regard to compounds that modulate sodium channels, undue experimentation would be required of the skilled artisan to practice the invention as broadly as it is claimed. As the specification provides no working examples of screening assays or compounds that affect SCN1A activity that have a therapeutic effect on any type of epilepsy or any neurological disorder, the skilled artisan would have to screen an extremely large number of different types of compounds to determine if a predictable correlation exists between any compound that "modulates" any SCN1A biological activity, or modulates inactivation of a sodium channel or activity of a sodium channel as it relates to SCN1A "functional fragments" or "allelic variants", and a therapeutic effect with regard to any epilepsy or any neurological disorder. The claims encompass an extremely large amount of experimentation requiring extensive trial and error analysis, the results of which are unpredictable. As such, the claims represent an invitation to experiment to determine if compounds that have any effect whatsoever on SCN1A nucleic acids, proteins, functional fragments or allelic variants are useful for treating epilepsy or any neurological disorder. Such experimentation is considered undue.

Conclusion

10. No claims are allowable.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name. It is also noted that after January 12, 2004, the examiner will be located at the new USPTO campus and will be reachable at telephone number (571) 272-0752.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne (Souaya) Sitton
Primary Examiner
Art Unit 1634

Jehanne Sitton
12/15/03